의학석사 학위 논문

프로칼시토닌을 이용한 세균성 폐렴과 방사선 폐렴 및 항암제 유발성 폐렴의 감별

Serum Procalcitonin as a Biomarker for Differentiation of Both Radiation Pneumonitis and Chemotherapy induced Pneumonitis from Bacterial Pneumonia

2014년 8월

서울대학교 대학원

임상의과학과

강 효 재

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지도교수 임재준

이 논문을 임상의과학과 석사 학위논문으로 제출함

2014년 7월

서울대학교 대학원

임상의과학과

강 효 재

강효재의 석사 학위논문을 인준함

2014년 7월

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외국어초록(Abstract)

Abstract

Title

Serum Procalcitonin as a Biomarker for Differentiation of Both Radiation Pneumonitis and Chemotherapy induced Pneumonitis from Bacterial Pneumonia

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Introduction

Procalcitonin is used as a promising biomarker for bacterial infection, especially bacterial

pneumonia (BP) in recent years. However, it has not yet been studied about differentiation of BP from non-infectious treatment-related pneumonitis (TRP), that is, both radiation pneumonitis (RP) and chemotherapy induced pneumonitis (CIP) using serum procalcitonin. The purpose of this study was to compare serum procalcitonin levels in patients with BP, RP and CIP, and to assess its diagnostic potential for discrimination of BP from both RP and CIP.

Methods

This study was a retrospective observation study. Among adult patients with suspected pneumonia who visited the National Cancer Center Hospital and underwent serum procalcitonin test as an initial pneumonia work-up from May 2012 through May 2013, procalcitonin levels in patients with BP, RP and CIP were compared.

Results

Among 220 patients with suspected pneumonia, 98 patients with non-classified pneumonia were excluded. Finally, 84, 29 and 9 patients were classified into BP, RP, CIP, respectively. Serum procalcitonin level in BP (5.64±18.97 ng/mL) was significantly higher than in RP (0.08±0.05 ng/mL) and CIP (0.14±0.12 ng/mL) (BP vs. RP: $p<0.001$ and BP vs. CIP: P=0.008. respectively, Mann Whitney (MW) test). In ROC curve analysis for discrimination of BP from both RP and CIP, serum procalcitonin had a higher diagnostic accuracy than CRP, fever (≥ 38℃) and BUN (area under the ROC curve (AUC) 0.935 *vs.* 0.835, 0.805, and 0.655, respectively). With a cut-off value of 0.19ng/mL, serum procalcitonin had a sensitivity of 90.5% and a specificity of 92.1% for discrimination of BP from both RP and CIP.

Conclusions

Serum procalcitonin level was very useful for differentiation of BP from both RP and CIP, so it would help avoid misuse of not only antibiotics for both RP and CIP but also steroid for BP.

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Keywords : Procalcitonin, Bacterial pneumonia, Radiation pneumonitis, Chemotherapy induced pneumonitis, Treatment-related pneumonitis

Student Number **: 2011-21962**

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Introduction

Procalcitonin has been recognized as a promising biomarker for bacterial infection, especially bacterial pneumonia (BP) in recent years.(1-7) In healthy subjects, procalcitonin is synthesized mainly in the C-cells of the thyroid gland as the precursor of calcitonin and its serum concentration is as very low as less than 0.1ng/mL. However, in patients with bacterial infections, it is produced by various organ and cells, such as lung, liver, kidney, pancreas, adipocytes and monocytes as well as thyroid(8-10) in response to primarily bacterial toxins and bacteria specific pro-inflammatory mediators, including interleukin 1ß, tumor necrosis factor, and interleukin 6.(3, 10) For these reasons, serum procalcitonin can be used as a useful marker for differentiation of BP from other infectious pneumonia or non-infectious pneumonia or pneumonitis. For example, serum procalcitonin levels in patients with viral pneumonia were significantly lower than in patients with mixed bacterial and viral pneumonia.(11) One study suggested that procalcitonin differentiate pneumococcal pneumonia from *tuberculosis* and *pneumocystis jirovecii* pneumonia(12) and the other study indicated that it differentiate acute exacerbation of interstitial pneumonitis from BP in patients with interstitial pneumonitis.(13)

In cancer centers such as the National Cancer Center (NCC), physicians frequently face trouble in differentiation of non-infectious treatment-related pneumonitis, that is, both radiation pneumonitis (RP) and chemotherapy-induced pneumonitis (CIP), from BP despite assistance of radiologic features or microbiologic tests or symptoms or signs in patients with pneumonia developed not long after receiving radiation therapy or chemotherapy. In case of BP, low diagnostic accuracy of microbiologic tests makes it difficult to identify causative agents, and in Korea, the causative organisms were found in only about 40% of patients with community acquired pneumonia.(14) In case of RP or CIP,

both diseases are diagnosed after exclusion of BP theoretically, even though clinical features such as radiologic findings suggest RP or CIP rather than BP. For these reasons, rapid differential diagnosis for the cause of pneumonia, especially, during early phase, can be hardly made. Thus, if there are effective biomarkers for differentiating RP or CIP from BP, physicians can choose more appropriate therapy between antibiotics and glucocorticoids. However, it has not yet been studied about the discrimination of RP or CIP from BP using serum procalcitonin level. Through this study, we aimed to compare serum procalcitonin in patients with BP, RP, and CIP, and to assess its diagnostic potential for discrimination of BP from both RP and CIP.

Methods

Study design and populations

This is a retrospective observational single center study. First, we selected adult patients with suspected pneumonia who visited the NCC and underwent serum procalcitonin test as an initial pneumonia work-up from May 2012 through May 2013. To be more specific, we enrolled the patients aged over 18 years who had newly developed symptoms of an acute lower-respiratory tract illness (cough and at least one other lower respiratory tract symptom) and/or at least one systemic feature (either a symptom complex of sweating, fever, shivering, aches, and pains and/or body temperature of 38℃ or more), had had new radiologic abnormality such as consolidation or ground-glass opacity (GGO) compatible with pneumonia on chest x-ray or CT image, and underwent microbiological tests for the diagnosis of bacterial pneumonia and serum procalcitonin test.(15) (16) Second, we excluded the cases that could not be classified into either BP or RP or CIP because of all negative microbiological tests and vague response to antibiotics or steroid, or the cases treated with antibiotics over 48 hours before procalcitonin test or the cases diagnosed with viral pneumonia, mycobacterial or fungal infection and co-development of BP and RP or CIP. Third, we classified the patients with suspected pneumonia into BP, RP and CIP, respectively, according to the criteria as follows. All cases were reviewed by two of the authors (HJ Kang and HS Lee) and classified into each pneumonia group. If there was a discrepancy in the judgment of two authors, it was adjusted by discussion of two authors.

Definition of BP

Patient with BP had had one of the two

- Positive results of microbiological study in blood, sputum, bronchoscopic specimens such as washing and BAL fluid, mycoplasma antibody, and urinary antigen of pneumococcus and *legionella*.(15) (16)
- Successful treatment response to antibiotics despite negative results of all microbiological study

Definition of RP

Patient with BP had undergone radiation therapy within 6 months before this pneumonia event and had all of these criteria (17)

- New consolidation or GGO on chest x-ray or CT image developed around radiation field
- Negative results of all microbiological tests
- Good treatment response to steroid
- Radiation fibrosis on chest x-ray or CT image of follow-up after proper treatment

Definition of CIP

Patient with BP had received chemotherapy agents with pulmonary toxicity within 6 months before this pneumonia event and had all of these criteria (18)

- Negative results of all microbiological tests
- Good treatment response to steroid

Procalcitoinin measurement

Samples were drawn from venous lines at the initial pneumonia work-up. Procalcitonin was assayed using time-resolved amplified cryptate emission technology on an analyser (Analytics E170, Roche Diagnotics, Penzberg, Germany) and functional assay (detection concentration 0.06 ng/mL). Total procalcitonin assay imprecision was reported by the manufacturer to be 10% at 0.20 ng/mL and less than 6% at more than 0.30 ng/mL.

Statistical methods

Data are presented as means ± standard deviation. Chi-square test was used to compare proportions for categorical variables. For continuous variables, Mann-Whitney test and Kruskall-Wallis test were used for comparing non-parametric data between two groups and between three groups, respectively. The diagnostic accuracy of biomarkers was examined by their area under the receiver-operating characteristic curve (ROC curve). Using ROC curves, we calculated the sensitivity and specificity at several cut-off points. Significance was accepted at the <0.05 level. Statistical analyses were performed with STATA statistical software (Version 9.0, Stata-Corp; College Station, TX, USA).

Results

Baseline characteristics of patients

During the period from May 2012 to May 2013, 220 patients in total took the procalcitonin test for pneumonia work-up. Total 98 cases were excluded (64 non-classified pneumonia, 28 BP treated with antibiotics over 48hours before procalcitonin test, 2 viral pneumomia, 2 tuberculosis, 1 NTM disease, 1 fungal pneumonia). Finally, 84 patients were classified as BP, 29 as RP, and 9 as CIP (Figure 1). Their clinical features are summarized in Table 1. There were no significant differences in age, gender, and underlying diseases among those three groups. Among basal laboratory tests, the blood urea nitrogen (BUN) and CRP were significantly higher in BP than in RP and CIP (P=0.020 and <0.001, respectively). Symptom of fever (≥ 38℃) was developed in 71% of BP patients, 3% of RP, and 33% of CIP patients(P<0.001). When the radiologic features of three groups were compared, consolidation (consolidation only + mixed consolidation and GGO) was found in 88% of BP patients, 72% of RT, and 22% of CIP. (P<0.001) All the patients with BP received antibiotics therapy and 7% of them steroid therapy as well since physicians could not exclude the possibility of RP or CIP. On the contrary, 93% of RP had steroid therapy, and 62% of RP had antibiotics therapy, too as physicians could not exclude the possibility of BP. All of the CIP patients received both steroid and antibiotics therapies together.

BP cases consisted of pneumococcal pneumonia, and *mycoplasma* pneumonia (Table 2). The rest of BP cases were diagnosed by clinical presumption depending on the response to antibiotics.

Figure 1

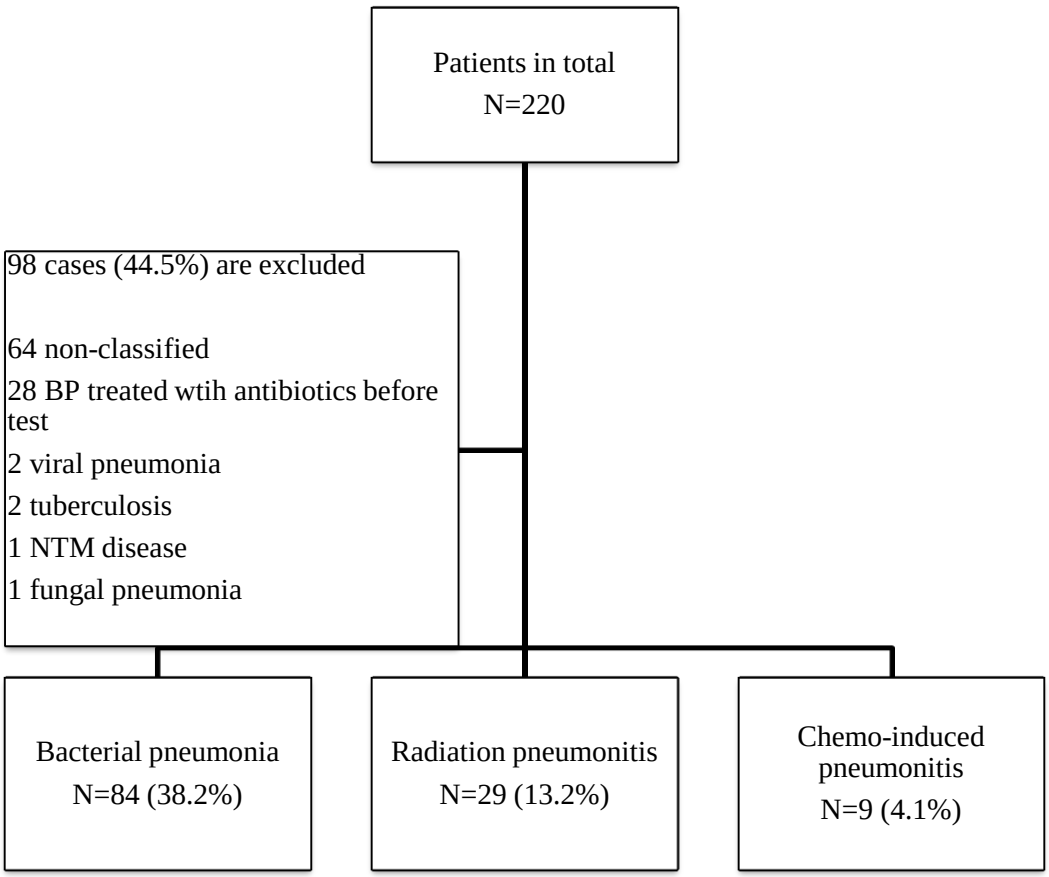

Patients in total
N=220
98 cases (44.5%) are excluded
64 non-classified
28 BP treated wtih antibiotics before test
2 viral pneumonia
2 tuberculosis
1 NTM disease
1 fungal pneumonia
Bacterial pneumonia
N=84 (38.2%)
Radiation pneumonitis
N=29 (13.2%)
Chemo-induced pneumonitis
N=9 (4.1%)

Table 1. Baseline characteristics of the patients with BP, RP and CIP

	BP N=84	RP N=29	CIP N=9	P-value
Age, mean (SD), y	65.87 (11.23)	68.13 (10.99)	70.30 (7.25)	0.381
Male, No. (%)	68 (81.0%)	19 (65.5%)	7 (77.0%)	0.234
Initial lab data, mean (SD)				
Leukocytes(x10³/μℓ)	8.99 (6.24)	7.09 (2.55)	8.47 (3.42)	0.270
Platelet (x10³/μℓ)	185.01 (110.52)	244.90 (99.92)	216.44 (91.39)	0.034
Segment neutrophil (%)	74.46 (19.03)	72.19 (11.41)	68.77 (13.32)	0.576
Blood urea nitrogen (mg/dL)	20.88 (11.75)	15.03 (5.20)	15.78 (5.82)	0.020
Serum creatinine (mg/dL)	1.06 (0.37)	0.99 (0.19)	1.05 (0.16)	0.587
C-reactive protein (mg/dL)	19.91 (10.35)	7.67 (8.70)	8.64 (7.17)	<0.001
Underlying disease, No. (%)				0.423
Lung cancer	46 (54.8%)	24 (82.8%)	7 (77.8%)	
Esophageal cancer	2 (2.4%)	0 (0%)	1 (11.1%)	
Breast cancer	5 (6%)	5 (17.2%)	0 (0%)	
Gastric cancer	2 (2.4%)	0 (0%)	1 (11.1%)	
Liver cancer	6 (7.2%)	0 (0%)	0 (0%)	
Hematologic malignancy	9 (10.7%)	0 (0%)	0 (0%)	
Head and neck cancer	2 (2.4%)	0 (0%)	0 (0%)	
Other cancer	9 (10.7%)	0 (0%)	0 (0%)	
Symptoms Fever ≥ 38℃, No. (%)	60 (71.4%)	1 (3.4%)	3 (33.35%)	<0.001
Radiologic features				<0.001

Consolidative or mixed type GGO-only type	74 (88.1%) 10(11.9%)	21(72.4%) 8 (27.6%)	2 (22.2%) 7 (77.8%)	
Use of the antibiotic therapy	84(100%)	18(62.1%)	9(100%)	
Use of the steroid therapy	6 (7.1%)	27 (93.1%)	9 (100%)	

BP; bacterial pneumonia, RP; radiation pneumonitis, CIP; chemo-induced pneumonitis, GGO; ground-glass opacity

Table 2. Result of microbiological culture study in bacterial pneumonia

Specimen	Total N = 84
Blood culture, No (%)	
Negative	81 (96.4 %)
Positive	3 (3.6%)
Streptococcal pneumonia	2 (2.4%)
Klebsiella pneumoniae	1 (1.2%)
Sputum culture, No (%)	
Negative	58 (69%)
Positive	26 (31%)
Pseudomonas spp.	5 (6%)
Klebsiella spp.	5 (6%)
Enterobacter spp.	2 (2.4%)
Enterococcus spp.	1 (1.2%)
MSSA	5 (6%)
MRSA	6 (7.1%)
Acinetobacter baumannii	2 (2.4%)
Mycoplasma Ag, No (%)	5 (6%)
Pneumococcal urinary Ag, No (%)	4 (4.8%)
Legionella urinary Ag, No (%)	0 (0%)

Procalcitonin levels in BP, RP and CIP

Figure 2 and Table 3 show the differences of the serum procalcitonin in BP, RP and CIP. Serum procalcitonin at baseline in BP (5.64±18.97 ng/mL) was significantly higher than in RP (0.08±0.05 ng/mL) and CIP (0.14±0.12 ng/mL) (BP vs. RP: p<0.001 and BP vs. CIP: P=0.008 and BP vs. RP/CIP; <0.001, respectively, MW test). But there was no significant difference between RP and CIP (p=0.08).

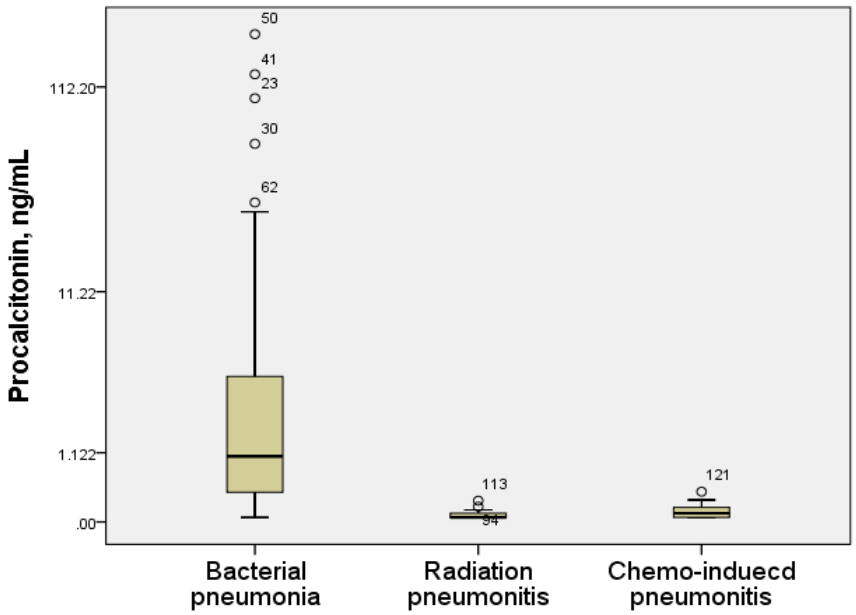
Table 3. Comparison of serum propcalcitonin levels in BP, RP and CIP

	BP N=84	RP N=29	CIN N=9	P-value*
Procalcitonin, mean (SD), ng/mL	8.98 (28.43)	0.08 (0.05)	0.14 (0.12)	BP vs. RP <0.001 BP vs. CIP 0.008 RP vs. CIP 0.08 BP vs. RP/CIP <0.001

*Mann Whitney test

BP; bacterial pneumonia, RP; radiation pneumonitis, CIP; chemo-induced pneumonitis

Figure 2. Comparison of serum procalcitonin levels in BP, RP and CIP



BP; bacterial pneumonia, RP; radiation pneumonitis, CIP; chemo-induced pneumonitis

ROC curve analyses of procalcitonin, CRP, fever, and BUN for discrimination of BP from both RP and CIP

Among possible predictors for differentiation of BP from both RP and CIP, procalcitonin was the best biomarker on the ROC curve analysis (Figure 3). In ROC curve analysis for discrimination of BP from both RP and CIP, serum procalcitonin had an AUC of 0.935, which was higher than that of CRP, fever (≥ 38℃) and BUN (0.835, 0.805, and 0.655,

respectively). (Table 4) The Diagnostic validity (sensitivity, specificity, PPV, and NPV) for discrimination of BP from both RP and CIP at different cut-off values are shown in Table 5. With a cut-off value of 0.25ng/mL, generally used for diagnosis of BP in several pneumonia guidelines, serum procalcitonin had a sensitivity of 85.7% and specificity of 92.1%. However, with a cut-off value of 0.19ng/mL, these values were elevated to 90.5% and 92.1%, respectively.

Figure 3. Receiver-operating characteristics (ROC) curve of Procalcitonin, CRP, Fever and BUN for discrimination of BP from both RP and CIP

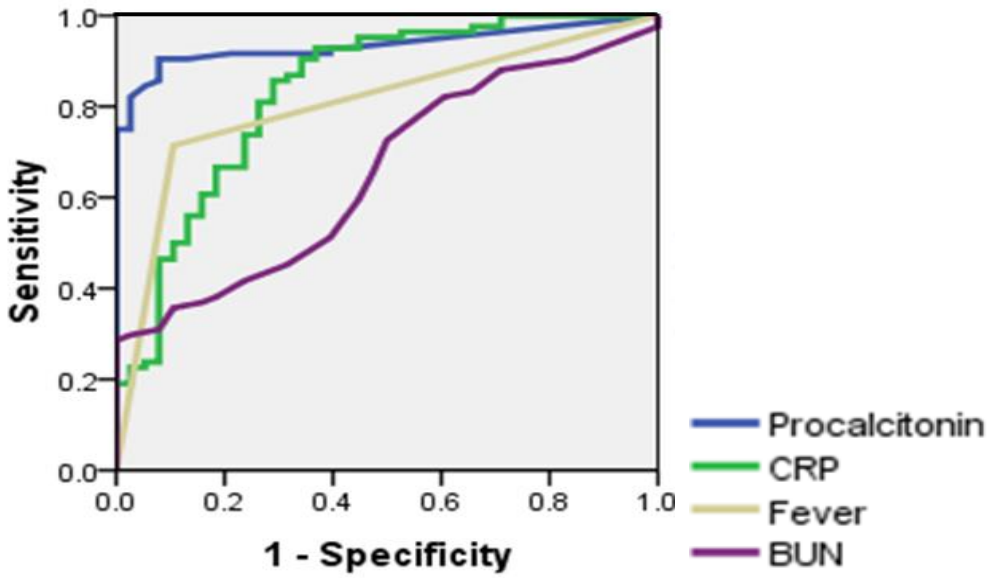


Table 4. The area under curve (AUC) analysis of Procalcitonin, CRP, Fever and BUN for discrimination of BP from both RP and CIP

	AUC	95% CI		P-value
		Lower Limit	Upper Limit	
Procalcitonin	0.935	0.891	0.979	<0.001
CRP	0.835	0.752	0.917	<0.001
Fever	0.805	0.722	0.887	0.006
BUN	0.655	0.555	0.754	<0.001

CRP; C-reactive protein, BUN; blood urea nitrogen

Table 5. Diagnostic validity of serum procalcitonin cut off test for discrimination of BP from both RP and CIP

(a) Cut off value of 0.25 ng/ml

	Estimated Value	95% CI	
		Lower Limit	Upper Limit
Sensitivity	0.857	0.760	0.921
Specificity	0.921	0.775	0.979
PPV	0.960	0.880	0.990
NPV	0.745	0.594	0.856

(b) Cut off value of 0.19 ng/ml

	Estimated Value	95% CI	
		Lower Limit	Upper Limit
Sensitivity	0.905	0.816	0.955
Specificity	150.921	0.775	0.979
PPV	0.962	0.885	0.990
NPV	0.814	0.661	0.911

BP; bacterial pneumonia, RP; radiation pneumonitis, CIP; chemo-induced pneumonitis; PPV; positive predictive value, NPV; negative predictive value

Discussions

This study showed that serum procalcitonin was a useful diagnostic marker for differentiation of BP from RP and CIP in cancer patients. To the best of our knowledge, this is the first investigation to identify the usefulness of serum procalcitonin for discrimination of BP from RP and CIP.

Treatment of BP is quite different from that of RP and CIP. That is, BP is mainly treated with broad-spectrum antibiotics. The role of corticosteroid in BP was limited, and especially, high-dose corticosteroid did not improve the outcome.(15, 16) Whereas, RP and CIP are mainly treated with high-dose corticosteroids.(17-19) Thus, differentiation of BP from RP and CIP is very important to make a plan for treatment. However, that is a very difficult task, even after all symptomatic, radiologic and laboratory data of patients are reviewed.

BP is the most common cause of pneumonia in patients who receive active treatment for cancer such as surgery, radiation therapy or chemotherapy. However, its diagnosis is not so easily made because the causative agent of infectious pneumonia was identified in only about 40 % of cases despite assistance of many microbiological tests.(14) In fact, blood cultures yielded positive results for a probable pathogen in 5%-14% in large studies of patients hospitalized with CAP,(15) so blood culture has too low sensitivity to confirm BP. Besides, sputum culture has too low specificity because of contamination and colonization.(15, 16) In addition, urinary antigen test for *pneumococcus* has moderate diagnostic rate (sensitivity 50%-80%; specificity of >90%), but the antibody test for *mycoplasma* has low diagnostic values. (15)

So, if all microbiological tests in patients suspected of BP show negative or unreliably

vague results, physicians cannot help diagnosing BP clinically after identifying the good response to antibiotics. As a matter of fact, this study showed that the causative agents were found in only 30 (36%) of patients with BP, and remained patients with BP were diagnosed by clinical presumption.

On the other hand, RP or CIP can be developed occasionally in cancer patients treated with radiation therapy or chemotherapy. For the diagnosis of RP and CIP, physicians should meticulously review the information on radiation therapy and chemotherapy, such as interval between treatment and pneumonia, radiation dosage, radiation field, types of chemotherapeutic agent etc., but basically, exclusion of infectious pneumonia is the most important.(17, 18) However, since more than half cases of BP have negative results of microbiological test, and furthermore, those results of microbiological tests, especially, sputum or blood culture study require considerable amount of time to come out, it is very difficult to differentiate both RP and CIP from BP at the initial phase of pneumonia. Besides, symptoms and radiologic features cannot completely distinguish both RP and CIP from BP. For example, although more than two thirds of patients with BP had a fever, a third of patients with CIP did. In an aspect of radiologic feature, 88%, 72%, and 22% of patients with BP, RP and CIP showed consolidation among abnormality patterns, respectively. (Table1)

For these reasons, when the patients get pneumonia during or after radiation therapy or chemotherapy, a physician should decide whether to treat the patients with antibiotics only or steroid only or combination of both as initial empirical treatment. In this study, we used antibiotics for all patients with BP from the beginning, but steroid was used only in 6 patients (7%) of them used steroid simultaneously as the possibility of RP or CIP could not

be excluded. On the contrary, in case of RP, 18 patients (62%) received antibiotics in addition to steroid, and only a third of patients with RP received steroid alone. Of 18 patients receiving both steroid and antibiotics, 10 patients were treated with combination of steroid and antibiotics at the same time as the possibility of BP could not be excluded, 4 received steroid within one week after use of antibiotics, and 4 received steroid over one week after use of antibiotics because of poor response to antibiotics. In case of CIP, all patients received both steroid and antibiotics simultaneously. (Table 1)

These empirical therapies for cancer patients with pneumonia have some problems. In case of using only one agent between antibiotics and steroid, if it is not a correct choice, that is, steroid for BP or antibiotics for RP or CIP, pneumonia will be aggravated. On the other hand, when combination of both antibiotics and steroid is used, in case of BP, inappropriate use of steroid therapy will induce aggravation of pneumonia, prolongation of treatment duration, and serum glucose elevation.(20) On the contrary, in case of RP or CIP, unnecessary use of antibiotics will induce emerging bacterial resistance to antimicrobial agents and the significant increase in *Clostridium difficile* infections, apart from the cost aspect of antibiotics use.(21, 22) Therefore, if the biomarker with ability to differentiate BP from both RP and CIP is available, physicians can avoid misuse of antibiotics or steroid.

C-reactive protein (CRP) is the most commonly used inflammatory marker for the patients with pneumonia until recently. However, it lacks specificity for the bacterial infections.(23, 24) In our study, CRP level was elevated in most patients with RP and CIP (mean±SD value, 7.67±8.7 and 8.64±7.1 mg/dl respectively). On the contrary, procalcitonin is not only a potentially more specific marker for bacterial infection, but also

shows the correlation with bacterial load and severity of infection.(25) Besides, serum procalcitonin levels are detectable as early as 3–4 h after bacterial infection, while CRP levels are elevated in 6-12hr after bacterial infection.(3, 26) Therefore, procalcitonin can make more rapid diagnosis of BP and can help physicians predict disease prognosis and decide the use of antibiotics.(1, 3, 4) As a matter of fact, this study showed that procalcitonin test was more useful for differentiation of BP from both RP and CIP than CRP (AUC of procalcitonin vs CRP = 0.935 vs 0.835, table 4).

According to current guidelines,(1, 3-5) a procalcitonin level over 0.25 ng/mL strongly suggests BP for patients who are suspected with BP, and antibiotic therapy should be initiated expeditiously for these patients. However, in this study, 12 patients (14%) of 84 patients with BP showed lower procalcitonin level with less than 0.25ng/mL. Most of them (10/12, 83.3%) were using steroid at the time of sampling of procalcitonin, and one patient was an immunocompromised host suffering from acute myeloid leukemia, and one had *mycoplasma* pneumonia. A few studies reported that procalcitonin level was not affected by steroid usage,(27, 28) but this study suggested that steroid usage or immunosuppressive state might affect production or release of procalcitonin. Several studies presented that in patients with BP caused by intracellular organisms such as mycoplasma, legionella, and chlamydia, procalcitonin level was relatively low compared with typical pathogens for BP such as pneumococcus.(12)(29, 30) In this study, among 5 cases with BP caused by mycoplasma, only one case demonstrated low procalcitonin level. While procalcitonin level in 14% of patients with BP was below 0.25ng/mL, the level in 92% of patients with RP or CIP was below 0.25ng/mL. Therefore, when cut-off value for discrimination of BP from both RP and CIP was set up as 0.19ng/mL, the best sensitivity and specificity were acquired. (Table 5)

There are some limitations in this study. First, it is a retrospective study using cancer patients who underwent procalcitonin test for initial work-up for pneumonia. Although procalcitonin test is performed for initial work-up for pneumonia in the NCC, some patients with pneumonia did not take procalcitonin test initially and were excluded in this study. Therefore, there might be a selection bias. Second, the number of patients enrolled is relatively too small to evaluate the usefulness of procalcitonin for discrimination of BP from RP or CIP, respectively. To address those limits, we are conducting the larger prospective study now.

In conclusion, serum procalcitonin level was very useful for differentiation of BP from both RP and CIP in patients who caught pneumonias during or after active treatment for cancers using cut-off value of 0.19ng/mL, so it would help to avoid misuse of steroid for BP as well as antibiotics for RP and CIP

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국문초록

요약(국문초록)

제목: 프로칼시토닌을 이용한 세균성 폐렴과 방사선 폐렴 및 항암제 유발성 폐렴의 감별

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목적

프로칼시토닌은 세균감염 혹은 패혈증이 있을 때 상승하며 특히 폐렴의 경우 바이러스 감염이나 비감염성 염증반응에서는 올라가지 않아 세균성 폐렴의 조기진단 및 질병 경과의 추적에 도움이 된다고 알려져 있다. 그러나 이 검사법이 세균성 폐렴을 비감염성 치료 관련 폐렴인 방사선 폐렴과 항암제

유발성 폐렴과 감별하는데 도움이 되는지에 대해서는 알려진 바가 없어, 이 연구를 통해 이들 질환의 감별에 대한 프로칼시토닌 검사의 유용성을 확인하고자 하였다.

방법

2012년 5월부터 2013년 5월까지 국립암센터에서 호흡기증상 및 영상학적 소견으로 폐렴 의심 하에 프로칼시토닌 검사를 시행 받은 환자들을 대상으로, 세균학적 검사 결과 및 폐렴 발생 6개월 이내의 방사선 치료나 항암치료 여부 및 치료 후 질병 경과를 분석하여 세균성 폐렴, 방사선폐렴, 항암제 유발성 폐렴 세 군으로 나누어 프로칼시토닌 검사 결과를 분석하였다.

성적

프로칼시토닌 검사를 시행한 환자 220명 중에 세균성 폐렴은 84명(38.2%), 방사선 폐렴은 29명(13.2%), 항암제 유발성 폐렴는 9명(4.1%), 기타 98명(44.5%)이었다. 세균성 폐렴, 방사선 폐렴, 항암제 유발성 폐렴 세군 간의 나이 및 성별에는 큰 차이가 없었다[남자 63명 (75%): 19명 (65.5%): 7명 (77.8%), P=0.57; 평균 나이 65.2±11.46세: 67.1±8.59세: 70.3±7.25세, P=0.36)]. 세균성 폐렴군의 평균 프로칼시토닌 레벨은 5.64±18.97였고 방사선 폐렴 환자는 0.08±0.05, 항암제 유발성 폐렴 환자는 0.14±0.12으로 방사선 폐렴 군의 평균 프로칼시토닌 레벨은 방사선 폐렴, 항암 유발성 폐렴군과 각각 통계적으로 유의한 차이를 보였다($p<0.001$, $p=0.008$, MW test). 그러나 방사선 폐렴과 항암 유발성 폐렴군 두군 사이에는 유의한 차이는 없었다($p=0.08$, MW test). 세균성 폐렴을 방사선 폐렴 및 항암제 유발성 폐렴을 포함하는 치료 관련성 폐렴과

감별진단하는 데에 있어 BUN, 38도이상 발열, CRP, 프로칼시토닌 등에 대한 ROC커브를 그렸을 때 세균성 폐렴 진단에 대한 프로칼시토닌의 AUC는 0.935로 CRP, 38도이상 발열, BUN (각각 0.835, 0,805,0,655) 보다 세균성 폐렴의 감별진단에 더 유리하였고 그때의 프로칼시토닌의 cut off값을 0.19ng/mL로 민감도는 90.5%, 특이도는 92.1%였다

결론

임상에서 세균성 폐렴과 방사선 폐렴 및 항암제 유발성 폐렴과의 감별이 필요할 때 프로칼시토닌은 매우 유용한 검사이다.

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주요어 : 프로칼시토닌, 세균성 폐렴, 방사선 폐렴, 항암제 유발성 폐렴, 치료 관련성 폐렴

학 번 : 2011-21962